Title of Project: Mindfulness-Based Cognitive Therapy for Preventing Suicide in Military Veterans

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1. Purpose/Specific Aims

We propose to conduct a randomized controlled trial (RCT) to test the efficacy of a psychotherapeutic intervention aimed at preventing suicidal behavior in veterans. The intervention, Mindfulness-Based Cognitive Therapy for Suicide (MBCT-S), was adapted by the present investigators from an existing evidence-based intervention for depression called Mindfulness-Based Cognitive Therapy (MBCT). The current intervention, MBCT-S, includes components specifically targeting reduction of suicidality. MBCT-S combines cognitive behavior therapy and mindfulness meditation practices into a unique, cost-efficient intervention that builds on the VA's existing Safety Planning intervention for veterans at risk of suicide. It adds an innovative transitional service model which begins therapy during inpatient care and continues post-discharge.

Important Note on Design: The current study will randomize veterans who are at risk for suicide to either Treatment-as-usual (TAU: control group) or MBCT-S + Treatment as usual (MBCT-S: experimental group). In the current study, TAU refers to the enhanced care and follow-up that is already part of VA standard care for veterans who are at risk for suicide. This includes assignment to a suicide prevention caseworker and increased frequency of mental health visits. Thus, the study's design is comparing what is already enhanced care (TAU) to care that is further enhanced with MBCT-S and all veterans will be receiving, at minimum, the VA's accepted enhanced care for suicide risk.

1.1 Objectives

1.1.1: To determine whether MBCT-S is more effective than Treatment as usual (TAU) in reducing suicide events, defined broadly as a range of suicidal behaviors identified in the VA's Self-Directed Violence Classification System (SDVCS). Our specific definition of a suicide event is described in the Measures section below.

1.1.2: To determine if MBCT-S is more effective than TAU in reducing suicide attempts.

1.1.3: To determine whether MBCT-S is more effective than TAU in reducing severity of suicidal ideation, depression and hopelessness.

1.2 Hypotheses

1.2.1: Compared to TAU: MBCT-S subjects will experience a longer duration from baseline until a suicide event.

1.2.2: Compared to TAU: MBCT-S subjects will experience a greater decrease in suicide events during the study period.

1.2.3: Compared to TAU, MBCT-S subjects will experience a longer duration from baseline until a suicide attempt.

1.2.4: Compared to TAU: MBCT-S subjects will have lower scores on the Beck Scale for Suicide Ideation, the Beck Depression Inventory and the Beck Hopelessness Scale.

2. Background and Significance

Strategies for reducing the risk of suicide are a top priority within the VA. Every month the VA becomes aware of approximately 1,100 veterans in VA care who attempt suicide. Although VA suicide prevention efforts seem to improve safety for some groups of veterans, VA data show that 11% of veterans with one suicide attempt make a re-attempt within 9 months.

There is a significant gap in the availability of evidence-based psychotherapies targeting suicide. While the VA has implemented most components of the multifaceted prevention approach recommended in a 2009 VA report on suicide,[1] it has yet to implement nationally any evidence-based psychotherapies targeting suicide. This gap may be due, in part, to the dearth of evidence-based therapies addressing suicide. The 2009 VA report, which identified only one small randomized controlled trial (RCT) with veterans and a handful with non-veterans, cited the pressing need for high-quality RCTs testing specialized therapies for those at suicide risk, a recommendation reiterated in a 2011 report commissioned by the Suicide Prevention Resource Center (SPRC),[2] which cited a "desperate" need for suicide-focused therapies.

Of the handful of RCTs for suicide therapies conducted to date, cognitive behavior therapy (CBT) has emerged as the most promising approach[3]. The psychotherapy to be studied in the current RCT, Mindfulness-Based Cognitive Therapy for Suicide Prevention (MBCT-S),[3] is a CBT approach that builds on an existing psychotherapy targeting depression, Mindfulness-Based Cognitive Therapy (MBCT). Both interventions integrate CBT approaches with "mindfulness," a Buddhist meditation technique found helpful in managing emotional dysregulation and other psychological processes underlying depression and suicidality. The investigators have adapted MBCT-S for suicide prevention by incorporating the VA's Safety Planning intervention and other mindfulness-based techniques specifically geared to addressing suicide risk. A short-term (8-week) group intervention, MBCT-S is cost-efficient, compatible with current VA suicide prevention strategies holds the promise of substantially reducing suicide risk in VA-connected veterans.

3. Research Design and Methods

Using a randomized controlled study design, the study will randomize 164 participants to receive either MBCT-S+TAU (n=82) or TAU only (n=82) in order to compare the adjunctive value of MBCT-S to the enhanced care currently provided to high risk for suicide patients. All consenting veterans meeting eligibility criteria will be enrolled in the study during the inpatient psychiatric admission associated with serious suicide ideation or a suicide attempt. As described in detail below, we will use broad inclusionary criteria in order to obtain a sample of patients who are diagnostically representative of those on the HRSL. Participants will receive a total of 5 assessments: (a) baseline (Time 1); (b) 4 weeks post-baseline (mid-treatment) (Time 2); (c) 8 weeks post-baseline (coinciding with MBCT-S treatment completion) (Time 3); (d) 6-months post-baseline (Time 4); and (e) 12-months post-baseline (Time 5). A 12-month follow-up will provide information on key outcomes that occur infrequently, such as suicide attempts,

and thus require a wider window for detection. In addition, data on suicide events and attempts will be obtained from patients' medical records at 12 months post-baseline *to verify self-report data*. We will use an intent-to-treat analysis to compare intervention and control group participants at each time frame.

Potential confounds that are known at baseline will be controlled for using the urn randomization method. This method balances the randomization based on predetermined indicators that could affect the outcome. Using this procedure, we will block the randomization according to: presence or absence of psychosis (either a psychotic diagnosis or one that includes psychotic features vs. no psychosis); and previous number of suicide attempts (none vs. 1+). Our randomized block design will thus classify participants into one of 4 blocks based on diagnosis (2 categories) and previous attempts (2 categories). We selected these variables in order to insure a balanced distribution of patient characteristics that might have effects on treatment engagement and/or outcomes.

3.1. Duration of Study

This is a four-year study that will actively recruit subjects for a period of approximately 3 years. Subjects will be enrolled into the study at the time of their hospitalization on the psychiatric acute unit for suicide-related behavior or risk and followed for 12 months post-study enrollment.

3.2 Study Sites

Subjects will be identified and enrolled into the study from the acute psychiatric units at the [redacted] and [redacted] campuses. The MBCT-S intervention will be delivered in individual sessions on both acute units and in group sessions at locations to be determined on both the Lyons and East Orange campuses.

3.3 Sample Size Justification & Subject Selection

The study will enroll a total of 164 subjects hospitalized on the [redacted] and [redacted] acute psychiatric units who qualify for inclusion on the VA's High Risk for Suicide List (HRSL). The study will only sample HRSL patients who experienced a hospitalization as a result of their index suicide event, which represents approximately 77% of all active HRSL patients. Approximately 8-10 patients are admitted to the acute units for suicide risk monthly. Over an approximately 36-month recruitment period, we expect to recruit approximately 3-5 patients per month to meet our enrollment goal.

Because our inclusion criteria are broad, we expect our sample to be representative of the population of HRSL patients hospitalized on the acute units. In FY 2011, this population was 85% male, 52% Caucasian; 33% Black; 8% Latino; and 4% Asian. The mean age was 47 (range=23 to 95). These veterans were diverse in terms of psychiatric diagnoses (non-mutually exclusive diagnoses include Depression-60%; PTSD-47%; Drug-related disorders-40%; Alcohol-Related disorders-38%; Bipolar Disorder-20%; and Schizophrenia-9%) and service era (Vietnam Era-29%; Post-Vietnam-25%; Gulf War-13%; OEF-OIF-25%).

To detect group differences on our principal measure, duration of time to first suicide event, we based our power analysis on prior literature and pilot data. Using the stpower cox command in Stata/MP 12.1 for Windows, which follows Hsieh and Lavori, [4] our power analysis estimated the required sample size to achieve 80% power at a 0.05 alpha level at a pre-attrition recruitment of 164 participants evenly

randomized at a 1:1 ratio to 82 per group. Based on our pilot data we assumed a hazard ratio of 0.421 and a control group failure probability of 32.1%; based on a comparable study by Brown et al., which reported an 18% attrition rate at 12 months, we assumed a 20% attrition rate, and used the standard deviation of the covariate of interest, group assignment, of 0.5. As noted, this analysis indicates we will need to recruit 82 subjects per group (total n=164) to attain a sample size of 66 per group (total n=132) after attrition. Moreover, we expect the study will be powered sufficiently to demonstrate clinical significance of the intervention as well. With respect to our main outcome measure, "duration of time to first suicide event," for example, our pilot data indicate the intervention may reduce by more than half the likelihood of a second suicide event within 12 months. This would translate into substantial savings in both human suffering and hospitalization costs.

3.4.1 Inclusion Criteria

3.4.1a: Subject is receiving treatment at the acute psychiatric care unit in East Orange or Lyons

3.4.1b: Subject's admission was associated with being placed on the HRSL **OR**
Subject was already on the high risk list and admission was related to suicidal ideation/behavior.

3.4.2 Exclusion Criteria

The following exclusion criteria were chosen to exclude Veterans who are unlikely to benefit from MBCT-S due to symptoms/difficulties that would curtail participation in the treatment or the ability to provide informed consent.

3.4.2 a: Subjects with cognitive deficits severe enough to decrease the likelihood of benefit from MBCT-S or to limit the ability to provide informed consent. Cognitive functioning will be assessed using items from the Brief Psychiatric Rating Scale and the impaired decision-making items from the VA consent form.

3.4.2 b: Subjects with severe symptoms of hallucinations or delusions

3.4.2 c: Subjects exhibiting disorganized or disruptive behaviors

3.4.2 d: Subjects who are medically unstable

The following exclusion criterion is to protect the study's internal validity:

3.4.2 e: Subjects who are currently receiving mindfulness-based psychotherapy or have received 2 or more sessions of a mindfulness-based psychotherapy in the last 12 months**.**

3.4.3 Subject Recruitment and Consent

Participants will be recruited within about 3-5 days of their admission to the [redacted] or [redacted] Acute Psychiatric Inpatient Units from among patients whose admission was related to a suicide event resulting in HRSL placement. Research staff will conduct daily review of acute psychiatry admissions at [redacted] and [redacted] and screen for admissions related to suicide risk. A study treatment clinician (defined as one of two VA psychologists who will deliver the MBCT-S intervention) will further review

the chart to confirm basic eligibility and consult with Suicide Prevention staff, if necessary. Eligible patients will be approached to request participation in the study by a study team member with clinical training and experience. Prior to approaching the patient, research staff will confer with the suicide prevention coordinators and/or with clinical staff on the acute units to insure that the patient is psychiatrically and medically stable and able to make an informed judgment about study participation. The study will be explained to the potential subject by the study research clinician, the consent will be read, and the subject's questions will be answered. Staff obtaining consent will clearly explain to the subject that their participation is purely voluntary and that they will not be denied their usual treatment services if they decline to participate. They will also be informed that they are free to withdraw from the study at any time with no adverse consequences to their receipt of treatment. Because the research will involve collecting periodic assessments of the patient's mental status, including intentions or behaviors involving self-harm, informed consent documents will also contain statements explaining mandatory reporting requirements for information regarding intention to harm self or others prior to participating in the study. Our safety plan for monitoring the risk of self-harm throughout the study is described in detail below in the section addressing study risks.

If the patient wishes to enroll, he/she will sign the consent form. If the patient wishes to further consider his/her participation, the research clinician will leave the consent form with the patient and make an appointment for a follow-up visit the next day, allowing the patient at least 24 hours to consider study participation. At the follow-up visit, if the patient wishes to enroll, he/she will sign the consent form. The study staff obtaining consent will also sign and date the consent form, and a copy will be given to the subject. All participating subjects will receive a copy of the VA's pamphlet regarding participation in VA research.

3.4.5 Subject Costs and Compensation

There will be no cost to subjects for the MBCT-S sessions. All subjects in the intervention group will be reimbursed for their treatment attendance according to the standard VA travel reimbursement rate of .415/mile. To retain group participants in the research component of the study, we will provide reimbursement of $30 per interview to both intervention and control group subjects for completing the research interviews. Other than travel costs, which will be reimbursed as described above, there are no expenses subjects are likely to incur as a result of their participation in this study.

3.5 Chart Review Selection

In addition to the chart reviews described above, which will be utilized to identify potential study subjects, research staff will also perform retrospective chart reviews on all enrolled study subjects for the purpose of identifying the occurrence of suicide-related "events" during the study follow-up period (12 months post-study enrollment). The definition of a suicide event is provided in our measures section below. In addition, retrospective chart reviews will be conducted in order to document treatments/medications other than MBCT-S provided to all study patients during the 12-month study time frame. Because our study occurs within the context of usual care, the following data will be collected to describe the usual care received and/or control for potential usual care covariates. We will extract retrospective data from patients' charts via the Data Access Request Tracker (DART), which is an online application developed and managed by the VA Informatics and Computing Infrastructure (VINCI). Upon receiving approval through the DART system, data will be extracted from the VA's National Corporate Data Warehouse and transferred electronically between the Transferring Agency and Custodian. Specifically, data will be transferred to Dr. Anna Kline via secure database-to-database

connection between the VINCI/CDW and VANJHCS servers. Both servers are behind the VA firewall and only accessible to authorized personnel. To obtain the extracted data, VA NJ research staff will provide VINCI with a "finder file." Subject Names, SSN, and ID numbers will uploaded to the secure server to enable the National Data Services staff to extract the requested data for the appropriate cohort. We will be requesting data pertaining to: a) VA outpatient mental health visits including treatment type and number of visits; b) inpatient mental health treatment episodes; c) prescription medications and pharmacy data. PHI/PII will be limited to scrambled SSN and treatment dates.
As with our primary data, all medical records data will have identifiers removed and data storage will occur by ID number, rather than name. Also, the data will be stored on a secure server that is maintained by the VA's IRM (Information Resource Management) and has up to date security protections. Within this server, the data will be placed on a secured folder [redacted] that is restricted for only users that are part of the VANJHCS Dual Diagnosis Unit, which is our local research unit. Within this access-restricted folder, we will store the data in a folder titled, "[redacted]."

4. Study Variables

4.1 Interventions

Treatment-as-usual We chose treatment-as-usual as our comparison condition in order to assess the relative value of adding MBCT-S to the VA's existing protocol of enhanced care for patients on the HRSL. According to VA policy, patients identified as being at high risk for suicide must receive 90 days of enhanced care from the time of their discharge from the acute unit or, for those not hospitalized, from the date they were "flagged." Specialized services during this time are provided by local suicide coordinators/case managers who help patients link to appropriate mental health and/or substance abuse services and assist in meeting the range of service needs patients may encounter in the community. During the 90 day period, patients are scheduled for a minimum of 4 weekly mental health visits for the first 30 days (at least one contact of which must be face-to-face), and at least one visit per month for the remaining three-month period. Patients are referred to services which best meet their specific needs and may include such services as substance abuse treatment, outpatient mental health care, or residential treatment. Suicide Prevention staff provide intensive follow-up of patients who fail to show for scheduled outpatient appointments if patients are believed to be in imminent risk of danger and often conduct outreach assessments/rescues in the community.

Once a patient is identified as high risk, the suicide prevention coordinator and patient together complete a suicide Safety Plan, which provides patients with a pre-determined list of coping strategies and resources to help lower their imminent risk of suicide. The basic components of the Safety Plan include (1) recognizing warning signs proximal to an impending suicidal crisis; (2) identifying and employing internal coping strategies; (3) utilizing contacts with people as a distraction from suicidal thoughts/urges; (4) contacting family members or friends; (5) contacting mental health professionals; and (6) reducing the potential for use of lethal means. Patients are instructed first to recognize when they are in crisis (Step 1) and then to follow Steps 2 through 5 as outlined in the plan. The Safety Plan was developed for the VA by Drs. Barbara Stanley, a Co-Investigator on this project, and Dr. Gregory Brown, in collaboration with Dr. Janet Kemp, also a Co-Investigator on this study.

MBCT-S. The proposed intervention was adapted to work in unison with the VA's current suicide prevention practices by incorporating into the standard MBCT program exercises that build on the VA Safety Plan to address the risk of suicide. If our intervention is found to be efficacious, we believe that

the integration of the intervention with existing strategies for suicide prevention will enhance its potential for implementation.

Approximately 5-10 participants will be enrolled per group. The standard MBCT program consists of 8 weekly 2-hour sessions, with daily home practice, including regular meditation and mindful movement practice for about one hour per day for 6 days a week. The core skill addressed in the standard MBCT protocol is the ability to "recognize and disengage from mind states characterized by self-perpetuating patterns of ruminative, negative thoughts."[3] Each class begins with a brief discussion of the theme and class curriculum, followed by in-class practice, and ends with a discussion of the immediate effects of the practice. MBCT-S maintains the same class structure and basic exercises as MBCT. In adapting the program for suicide, MBCT-S focuses primarily on Safety Plan Steps 1 and 2, providing exercises aimed at promoting patient awareness and recognition of the warning thoughts, feelings and situations identified as triggers on the Safety Plan (Step 1) and identifying and using positive internal coping responses (the mindfulness "skillful response") to these warnings (Step 2). Each patient uses their own Safety Plan, with specific triggers they identified in conjunction with their suicide prevention case manager. The identification of triggers may be further enhanced during group and individual MBCT-S sessions. MBCT-S classes will be led by two clinical psychologists. Both clinicians have been collaborating as part of our team in developing and delivering mindfulness-based interventions.

MBCT-S is designed to achieve a transitional model via its session structure, which involves two individual sessions in the inpatient setting and 6 group outpatient sessions. We expect MBCT-S to promote continuity between inpatient and outpatient treatment phases by establishing a therapeutic alliance prior to the inpatient-outpatient transition that will be relied upon to improve outpatient engagement. The first 2 individual inpatient sessions are geared to introducing the patient to the program and the basic concepts of mindfulness, reviewing each patient's personal Safety Plan, enhancing the identification of suicide triggers identified on the Safety Plan, introducing the application of mindful awareness of suicide triggers and providing personalized guidance on establishing a home practice. The remaining group outpatient sessions are devoted to enhancing the ability to apply mindfulness to the thoughts, feelings and situations likely to trigger suicidal thinking.

MBCT-S adopts a patient-centered model in a number of ways. Unlike purely group-based approaches, MBCT-S's initial use of individual sessions provides a phase where the treatment rationale and goals can be individualized. This will rely heavily on tying the treatment to the Suicide Safety Plan, which is itself highly individualized. Patient-centeredness is also achieved through a design that is compatible with the population's needs and preferences. The VA's own data show that veterans at risk of suicide demonstrate significant difficulty engaging with treatments that are long-term and of high intensity, with no VISNs meeting the annual high risk suicide performance monitor for required mental health visits as of October, 2011. Thus, MBCT-S, which is shorter term and partially completed prior to discharge, was in part selected to better match the treatment utilization patterns of this population. Moreover, the intervention was specifically designed to address the challenge of outpatient continuity among patients with a myriad of presenting problems. Achieving this type of continuity requires an engagement-oriented approach that emphasizes patient support.

4.1.1 Drug or Device Interventions

None

4.2 Dependent Variables or Outcome Measures

Our primary outcome/dependent variable is **suicide "events**," including both attempts and serious ideation. While we will also examine **suicide attempts** as a secondary outcome, we are limiting our primary outcome to events because of the anticipated low incidence of attempts during our 12-month follow-up period.

We are defining both events and attempts according to the VA's standardized Self-Directed Violence Classification System (SDVCS). An "event" will be defined as the occurrence of one or more of the following: (a) suicidal ideation with suicidal intent, with or without a specific plan; (b) preparatory behaviors; (c) deliberate self-directed violence, with or without injury, including actual attempts or attempts that are interrupted or aborted, in which evidence of intent is either indeterminate or clear. Suicide attempts, defined according to the SDVCS, will include deliberate self-directed violence that: (a) is actual or interrupted by self or others: (b) results in injury or the potential for injury; (c) includes evidence of suicidal intent which is explicit, implicit or unclear. We will operationalize the above definition of suicide events and attempts using the Columbia Suicide Severity Rating Scale (C-SSRS).

In addition to measuring differences between treatment groups with respect to the above outcomes, we will also explore the effect of treatment group on measures of **suicide ideation**, **depression** and **hopelessness.** Suicide ideation will be measured utilizing two instruments – the Beck Scale for Suicide Ideation, which is the gold standard for ideation measurement and provides a dichotomous (yes-no) measure of the presence or absence of ideation, and the C-SSRS, which provides a measure of ideation severity. Depression will be measured utilizing the Beck Depression inventory and hopelessness, the Beck Hopelessness Scale. In addition, we will use the MINI International Neuropsychiatric Interview (MINI)[5] to obtain a standardized psychiatric diagnosis and subscales from the Brief Psychiatric Rating Scale to screen patients for eligibility at study enrollment. We will also administer the Experiences Questionnaire to assess the acquisition of mindfulness skills as a result of the intervention. The instruments and data sources we will utilize to measure these outcomes, along with the timeframes for instrument administration/data collection, are described below.

Columbia Suicide Severity Rating Scale [6](C-SSRS) will be used at baseline and at each follow-up point to measure the occurrence of our two primary outcomes: a *suicidal event* and a *suicide attempt.* Designed to quantify the severity of suicidal ideation and behavior, the scale provides information on the presence or absence of active suicidal thoughts, method and/or intent and severity of ideation, determined according to such factors as frequency, duration, controllability, deterrents and reasons. The scale also assesses self-injurious behavior, whether the behavior was interrupted or aborted, preparatory acts and the actual and potential lethality of the behavior. In three multisite studies with adolescents and adults, the C-SSRS demonstrated good convergent and divergent validity with other multi-informant suicidal ideation and behavior scales and had high sensitivity and specificity for suicidal behavior classifications compared with another behavior scale and an independent suicide evaluation board.

Beck Scale for Suicide Ideation[7] (SSI) In addition to the C-SSRS, we will use the SSI as a separate measure of *ideation severity.* The 21-item clinician-administered SSI, administered at baseline and at all follow-ups, is one of the most widely-used measures for detecting and measuring the intensity of the patients' attitudes, behaviors, and plans to commit suicide during the past week. The SSI has been standardized

with adult inpatient and outpatient psychiatric patients, including men and women of diverse racial/ethnic backgrounds and ages. It has demonstrated moderately high internal consistency, with Cronbach coefficient alphas ranging from .84 and high inter-rater reliability, with correlations ranging from .83 to .98. The SSI is significantly associated with suicide items from the Beck Depression Inventory and the Hamilton Rating Scale for Depression as well as with previous suicide attempts and depression severity, discriminating suicidal inpatients from depressed outpatients and suicide attempters from non-attempters**.**

Beck Depression Inventory-II [8] The BDI-II will be used at baseline and follow-up to measure severity of current depressive symptoms pre- and post-treatment. The BDI-II contains 21 statements, assessing symptoms over the preceding two weeks. Beck, Steer, and Brown report excellent internal consistency in both patient and student samples. A meta-analysis of the BDI's internal consistency estimates from more than 20 years of use yielded a mean coefficient alpha of 0.86 for psychiatric patients and 0.81 for non-psychiatric subjects.[8] The concurrent validity of the BDI relative to clinical ratings and the Hamilton Psychiatric Rating Scale for Depression were 0.72 and 0.73, respectively, for psychiatric patients and 0.60 and 0.74, respectively, for non-psychiatric patients. Recent evidence indicates that the BDI discriminates subtypes of depression and differentiates depression from anxiety.

Beck Hopelessness Scale (BHS) [9] We will administer the Beck Hopelessness Scale (BHS) at baseline and follow-up to explore the effects of the intervention on feelings of hopelessness, a strong correlate of suicidality. The BHS is a 20-item true-false scale for measuring negative attitudes about the future. Research consistently supports a positive relationship between BHS scores and measures of depression, suicidal intent, and ideation. In a population of 294 hospitalized patients with recent suicide attempts, the internal consistency of the scale, analyzed by means of coefficient alpha (KR-20), yielded a reliability coefficient of .93. All of the 190 coefficients in the inter-item correlation matrix were significant, and highly significant correlations were obtained between each item and the total BHS score, with item-total correlation coefficients ranging from .39 to .76. The concurrent validity between the BHS, clinical ratings of hopelessness and other measures of negative attitudes about the future were also high. The correlations of BHS total scores with clinical ratings of hopelessness in a general outpatient medical practice and in 62 hospitalized patients with recent suicide attempts were 0.74 ($p<.001$) and 0.62 ($p<.001$), respectively. Correlations with the Stuart Future Test and the pessimism item on the BDI were 0.60 *($p < .001$)* and 0.63 *($p<.001$),* respectively.

Experiences Questionnaire[10] We will use the 11-item decentering factor from the Experiences Questionnaire, a measure designed by the developers of MBCT, to assess the extent to which the intervention helps participants to decenter or disengage from the content of negative thinking, a primary clinical goal of MBCT and MBCT-S. The measure will be administered to all participants at baseline, mid-treatment and immediately post-treatment. Sample items, which include, “I can observe unpleasant feelings without being drawn into them” and “I notice that I don’t take difficulties so personally,” are rated on a 5-point Likert scale. In clinical and non-clinical samples, the convergent and discriminant validity of the decentering factor was demonstrated in negative relationships with measures of depression, rumination, experiential avoidance, and emotion regulation. The EQ factor structure was replicated in a clinical sample of individuals in remission from depression, and the decentering factor evidenced a negative relationship to concurrent levels of depression symptoms. Patients with major depressive disorder (MDD) scored significantly lower on this factor than healthy controls, with an effect size exceeding conventions for a large effect: ($F (1, 117) =50.32$, $p<.0001$, $d=1.31$). Levels of decentering among MDD patients were significantly and negatively correlated with concurrent self-report ($r=-.46$) and clinician-assessed ($r=-.31$) levels of depression symptoms.

The Mini International Neuropsychiatric Interview (MINI) [5] The MINI is a brief structured interview that assesses the criteria for DSM-IV Axis I diagnoses (e.g., anxiety, mood, and substance abuse disorders). The MINI has been shown to concur with diagnoses obtained using the Structured Clinical Interview for DSM-IV Disorders. [5] For the present study, the MINI was used to assess for the presence of diagnoses in the following diagnostic classes: psychotic, substance, mood, anxiety. The MINI has the advantage of having approximately half the time required to administer, compared with the SCID, yet also generating diagnoses that concur with the SCID. The shorter administration time is expected to decrease participant burden. The MINI will only be administered during the baseline (T1) assessment.

4.3 Risk of Harm and Protections Against Risk

The proposed study involves non-invasive interview assessment measures and a psychosocial intervention, both of which are associated with minimal risk. However, because all study participants have a history of suicide ideation and/or attempts, this study will include special precautions to insure the safety of patients during both the treatment and research phases. The risk associated with each component of the research is outlined below, followed by the steps we will take to minimize these risks.

Structured Interviews, Rating Scales, Questionnaires, and Electronic Medical Record Review:
These types of assessment procedures are commonly used in psychiatric research and are generally associated with minimal risk. Given the high risk status of our sample, however, there is a possibility that participants may become distressed during the assessments due to the sensitive nature of the subject matter or may make statements or report behaviors indicating deteriorated psychological status unrelated to their study participation. To address problems that might arise during research assessments that are either related, or unrelated, to the study, all assessors will receive formal training and supervision on suicide risk assessment and suicide crisis procedures from study Co-Investigator Dr. Barbara Stanley, an international expert on suicide prevention and developer of the VA's safety planning intervention. The use of trained professionals as assessors (e.g., master's level social work or psychology research assistants and/or research assistants with significant experience administering psychosocial assessments to patients at risk of suicide) will further ensure that any potential safety issues are identified and appropriate interventions are undertaken. Our safety procedures for ensuring appropriate follow-up with patients exhibiting enhanced risk are described below.

If a study participant is determined to be at imminent risk for suicide during a telephone follow-up assessment, the assessor will immediately contact 911 to initiate an on-site rescue if such action is clinically indicated. If, based on clinical impression, a patient appears to be at elevated but not imminent risk of suicide during a follow-up phone assessment, several steps will occur. Assessors will contact the local suicide prevention coordinator, the senior study mental health professional – Ph.D., M.D. level – to whom responsibility has been delegated, and the study PI to notify them of the situation. If clinically indicated, research staff will initiate a transfer to the VA National Veterans Suicide Prevention Hotline in Canandaigua, NY, as per recent national directives. Assessors will have emergency contact information available at all times for the senior study mental health designee, local suicide prevention coordinators and emergency services (e.g. VA National Veterans Suicide Prevention Hotline in Canandaigua, NY). As clinically indicated, assessors will stay on the telephone with the participant until they are able to consult with the study mental health professional and/or local suicide prevention coordinator, determine next steps, and follow-through with them. The patient's regular VA treating clinician will also be notified of any emergency events or significant changes in mental status.

At the end of the follow-up assessment, all participants regardless of risk status will receive the VA Suicide Prevention Hotline telephone number to keep with their records and will be reminded of this number at each follow-up assessment contact.

There is also a possibility that during the MBCT-S intervention, the therapy may intermittently address sensitive personal issues that result in emotional distress experienced during the group therapy sessions. Both study therapists are highly experienced in the clinical management of psychological and behavioral problems associated with suicidality, however, and will insure that appropriate measures are provided to minimize patient distress. If patients become dangerously suicidal during the group sessions, their treating clinician will be notified and the study clinician will escort the patient to the [redacted] ED or [redacted] Walk-in clinic for immediate care.

In addition to the safety risks associated with conducting research with patients at risk of suicide, the other primary foreseeable risk is associated with breaches of confidentiality of study data or personal information.

In order to protect the privacy of participants, we will closely adhere to VA regulations. The recruitment process will entail the use of a contact spreadsheet that contains protected health information (name, social security number, diagnostic data and notes on suicide risk). This administrative spreadsheet will be stored separately from the study's research data. No protected or personal health information will ever be recorded or stored in a permanent research database. The contact spreadsheet will be placed on a secure VA server. The spreadsheet will not be downloaded to a personal computer and will only be used by authorized members of the research team for the purpose of recruitment. The database containing demographic information and interview responses is separate and will therefore never contain protected health information. This process insures that protected health information is never recorded in the research database. The data will be destroyed following the release of VA regulations on retention of research records and will follow the VA's policy for destruction of study records.

With respect to other data, all paper-based information containing personal identifiers (such as consent forms) collected in this study will be kept in locked filing cabinets accessible only to the research staff of the VA NJ Health Care System. All assessment data will be collected in a private VA office and directly input into a computer database and stored in password-protected VA files on the secure VA server. Assessment data will be identified by ID number only and will not be associated with any personal identifying information. The database that contains the link between the subjects' names and their ID numbers will be maintained on a separate password-protected spreadsheet on the secure VA network. The final research database will not contain any PHI. No personal identifying information will be included in published findings from the study or in reports to the funding agency. The specific time frame for destruction of identifiers will be determined following the release of VA regulations on retention of research records and will follow the VA's policy for destruction of study records.

In addition to the above data, we will also be audio-recording approximately 20% of MBCT-S group sessions for the purpose of conducting fidelity reviews to ensure clinicians are following the MBCT-S protocol in delivering the treatment. Voice recordings are Personal Health Information as they can be used to identify an individual; however, individuals will not be identified by name on the group session recordings. Participants will be aware that some sessions will be recorded and will be requested to provide permission for the recording at the time of consent. Following each recorded session, we will immediately transfer the recordings from the digital recorder to the VA server and the audio file will be assigned a code name. The recording will be deleted from the original device according to VA protocol.

The digital recorder will be kept in a locked cabinet in the VA office of the interviewer. The code name assigned to the audio file will identify a particular treatment session and will not include any information that could in any way be linked to the names of the session participants.

Loss of confidentiality may also occur as a result of the group nature of the intervention, with patients inadvertently violating the confidentiality of information revealed by others in the group. To avoid this possibility, participants will be educated about expectations regarding respecting other group members' confidentiality and limits to confidentiality. Standard instructions to groups that what is said during the group is confidential and must stay within the group and not be talked about with anyone else outside the group will be given. Such group interventions are commonly used in standard care, so the level of risk is not increased from the standard of care.

4.4 Potential for Benefit

Participation in this research program may have the potential to provide direct benefit to the intervention participants. Participants receiving the intervention may indeed acquire skills that will improve their ability to manage their mood and suicidal thoughts, potentially leading to a significant reduction in suicide risk. Participants randomized into the control condition will still receive the same enhanced VA treatment and care they would have received otherwise. In addition, the findings from the current study have the potential to fill a much-needed gap for the treatment of suicidal risk among patients being discharged from an inpatient psychiatric facility. All participants, regardless of study group will also receive assessments at five different time points, which will serve as an additional contact for the participants and will provide for additional monitoring of their status. The benefit of this will be an increased capacity to detect and respond to a mental health need.

5. Data Handling and Statistical Analysis

Overall, statistical significance will be defined by a p-value < 0.05, unless specified otherwise. Bonferroni corrections will be applied to multiple testing, as appropriate. Prior to conducting an analysis of group differences as a result of a treatment effect, we will first examine baseline group differences to determine the success of the urn randomization procedure in achieving between-group equivalence and detect any baseline differences that could bias study findings. Chi-square analysis and Student's t-test will be used, as appropriate, to examine demographic variables, previous suicide attempts, psychiatric diagnosis and service era for non-equivalence between MBCT-S and TAU. Given that the RCT occurs within a naturalistic treatment context (i.e., VA usual care for HRSL patients), possible group differences in subsequent access to, and number of, VA TAU psychotherapy and psychopharmacology sessions will also be explored. To protect against a Type II error, a criterion of $p < .10$ will be used to identify potential confounders. If potential confounders are identified, they will be entered as covariates in the respective analyses described below.

We will also employ methods to examine the possible effects of both therapist and site on study outcomes by testing for nesting effects in our models. For the therapist variable, we will use a partially nested design$_{11}$, since therapist effects will be analyzed for treatment group participants only. In the case of mixed-effects models, therapist and site variables will be entered as fixed effects since the limited number of therapists and sites in the proposed study (2 each)$_{12}$ constrains the generalizability of inferences that could be derived from specifying random effects. We have modified the description of our analyses below to specify how we will test for site and therapist effects in each case.

For H1a, survival time analyses to compare MBCT-S to TAU will be run once at 12 months post-baseline using the Cox proportional-hazards regression model to test for group differences in the time from baseline to first in-study suicide event. Site will be entered as a nesting factor into the regression. For the therapist variable, we will test for a partially nested effect, simplifying assumptions regarding the patterns of clustering related to the use of a primary therapist or primary group. The regression analysis will also allow us to control for censoring effects due to the differential length of follow-up or the completion of follow-up without a repeat suicide event. However, if the proportional hazard assumption is not met, we will utilize other approaches to survival analysis, such as the log-rank test.

For H1b, we will obtain a count of "suicide events" during each assessment period, including baseline. Given that suicide events occur infrequently and have a non-normal distribution, a mixed-effects Poisson regression will make a between-group comparison with events as the dependent variable, one between-group variable (MBCT-S vs. TAU), one repeated factor for the multiple assessments, and a group by time interaction. The model will specify intra-subject correlation as a random effect nested within site (which will be specified as a fixed effect) and we will test for a partially nested effect for therapist as specified above. We will consider several correlational structures between repeated measures (e.g., compound symmetry) and determine the best structure using the Akaike's Information Criterion (AIC). Potential confounders that meet the $p<0.10$ criterion stated above will be entered as covariates.

For H_{2a} analysis will be similar to that described in H1a. Specifically, Cox proportional-hazards regression model analyses will be run at 12 months post-baseline to analyze and compare across groups the survival-time to the first suicide attempt.

For H_{3a} we will measure suicidal ideation using two scales – the Beck Scale for Suicide Ideation (SSI) and the Columbia Suicide Severity Rating Scale (C-SSRS). The SSI is the gold standard for measuring suicide ideation and will provide data that has comparability to other studies. The SSI, however, only allows calculations of suicide severity for those screening positive for ideation and so produces scores that tend to be highly skewed. For that reason, we are using the SSI to determine presence or absence of ideation, but will also use the C-SSRS to measure severity of ideation since it allows all subjects to be included in the analysis. The C-SSRS severity scale ranges from 0 "no ideation present" to 5 "active ideation with plan and intent." Similarly, intensity of ideation will be measured using the C-SSRS intensity scale, which ranges from 0 "no ideation" to 25 "most intense."

The analysis for H3a will examine 3 aspects of suicide ideation - presence of active ideation, ideation severity and ideation intensity. Our first analysis will treat ideation as a dichotomous variable (present or absent), with a response of "0" on both SSI screening items indicating absence of current ideation. We will use random effects logistic regression with repeated measures to test for between-group differences in the occurrence of suicide ideation in the previous time period. The model will include one between-group variable (MBCT-S vs. TAU), one repeated measure (Times 1-5), and group by time interactions to assess for between-group differences during the five time periods. The model will specify intra-subject correlation as a random effect nested within site (which will be specified as a fixed effect). As described above, therapist will be treated as a partially nested fixed effect. Potential confounders will be entered as covariates and linear contrasts will test if MBCT-S produces greater reductions than TAU in the occurrence of suicide ideation at each time period.

For severity of ideation, we will use mixed models analysis to make between-group comparisons with "severity of ideation" as the dependent variable, one between-group variable (MBCT-S vs. TAU), one repeated measure (Times 1-5), and group by time interactions. We will consider several correlational structures between repeated measures (e.g., compound symmetry) and determine the best structure using the Akaike's Information Criterion (AIC). Potential confounders that meet the $p<0.10$ criterion stated above will be entered as covariates. Linear contrasts will test between-group differences in "severity of ideation" separately at each time point. The same mixed models analytic strategy will be used to assess "intensity of ideation," with "intensity" as the dependent variable, MBCT-S vs. TAU as the between-group variable, the five time periods as the repeated measure and group by time interactions. As in the analysis for severity, we will determine the best correlational structure between repeated measures, test for confounders as appropriate and use linear contrasts to test between-group differences in "intensity" at each time point. For both severity and intensity, as well as for all remaining mixed models analyses described below, we will control for site as a nested fixed effect and therapist as a partially nested fixed effect.

6. Data and Safety Monitoring

In addition to the detailed measures described above to maintain the safety of research participants and their data, this study will have a Data and Safety Monitoring Board (DSMB), which will serve as an oversight committee, reviewing any modifications to the research design and conduct of the study and making recommendations according to the NIH Policies for data and safety monitoring as described below. Definition of Adverse Events and Serious Adverse Events will be determined in accordance with the DSMB and the IRB. Reports of adverse events will be made to the IRB according to the standards for expedited reporting.

The individuals who will serve on the DSMB are: [redacted]

The specific goals of this joint DSMB are:
1. To review new or modifications to risk management protocols at both sites.
2. To review procedures and decisions regarding the adequate protection of specific patients when investigators move into risk management protocols because of adverse events or clinical deterioration.
3. Review progress toward meeting enrollment goals.
4. To review procedures for maintaining the confidentiality of data, and quality of data collection, management, and analyses.
5. When appropriate, serve as final arbiters of whether individual patients should be removed from a protocol.
6. To recommend continuation, discontinuation, modification, or termination of a study based on emerging data (in the study and literature) and evaluation of risk/benefit ratio.
7. To conduct annual reviews to determine whether patient safety has been adequately safeguarded.
8. To meet at least once yearly with the principal investigator to review progress reports.

The general purpose of the data monitoring plan will be to maximize the safety and privacy of all study participants, and ensure the integrity, validity, and confidentiality of the data collection and analysis procedures. These objectives will be accomplished through regular monitoring and oversight by the Principal Investigator. The Principal Investigator will report any serious and unexpected adverse events

and unexpected problems that involve risk to the participants or others, or any breaches in confidentiality to the Institutional Review Board (IRB).

Each year, the PI will include a summary of data safety monitoring activities in the annual progress reports to the IRB. These reports will include: (1) whether participants' safety, privacy and confidentiality has been consistently assured by the investigators; (2) review of interim data analyses that bear on outcomes of the study and risk/benefit ratios to participants, including recommendations for new statistical analyses; (3) judgment as to whether research instruments have been administered in a uniform manner and in a way that maintains the participants' privacy; (4) a review of the study's progress toward recruitment goals, quality of data (e.g., appropriate completion of forms), and participant retention/attrition rates; and, (5) a review of new scientific literature pertinent to the safety of participants or ethics of research participation.

There will be regular, ongoing communication between the PI and the local IRB. While no serious and unexpected adverse events are expected as a result of participation in the research study, any unanticipated study problems will be reported to the local IRB. The study psychologists will take all clinically appropriate actions to prevent and treat psychiatric emergencies in participants.

7. Reporting Results

We will not be conducting medical tests or collecting any other measures that would require patient notification. In terms of professional reporting, aggregate results will be reported in a final report to the funding agency as well as in presentations at professional meetings and in peer-reviewed journals.

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Protocol Amendments

The following amendments were made to the original protocol before participant recruitment began:

1. 10-21-13:
First, we added the Five Facets of Mindfulness Questionnaire short form, the Stroop Neuropsychological Test, the Go-no-go Inhibition task, the Suicide Related Coping Measure, 17-item PTSD Checklist, the Distress Tolerance Scale, Barrett Impulsivity Scale, and the Brown-Goodwin Lifetime Aggression Scale and removed the Brief Psychiatric Rating Scale and Experiences Questionnaire. Second, we edited hypothesis 1.2.4 to include that MBCT-S participants would have lower scores on the Beck Scale for Suicide Ideation, the Beck Depression Inventory and the Beck Hopelessness Scale. Third, we will randomize using Excel as the URN randomization is not compatible with Windows 7 at VANJ. Fourth, there will be 8 weeks of group intervention, not 6. Fifth, as the T2 and T3 assessments are intended to capture information at mid and post treatment, respectively, the time 2 survey will be conducted at 6 weeks post-baseline as opposed to 4 weeks, and the time 3 survey will be 3 months post-baseline, not 8 weeks. Sixth, we changed the subject incentive payment schedule from $30 per assessment to $20 for the first assessment, $25 for the second, $30 for the third, $35 for the fourth and $40 for the fifth assessment in order to incentivize study completion. Last, we created a “completely interviewer-administered" version of the survey for cases where interviews may need to be administered over the phone.
2. 11-22-13:
We added a brief (3-minute) word recognition memory task to our neuropsychological assessments to investigate if differences exist between those who attempt suicide vs. those that do not, as previous studies have suggested. Additionally, we modified treatment delivery requirements to allow for outpatient individual sessions if necessary, as many eligible Veterans have brief inpatient stays.

The following amendments were made after the first participants had enrolled:

3. 1-24-14:
We expanded inclusion criteria for our study to include Veterans who have current and active high risk for suicide flags who are either currently hospitalized without current suicidal ideation or who had mental health related hospital treatment within the past month. Next, we changed our Time 2 and Time 3 assessments to line up with mid and post-treatment, respectively, rather than with a fixed time point. to allow us to better support our research hypotheses as each participant will have received the appropriate number of treatment sessions prior to their mid and post treatment assessments. Control

subjects will be matched with treatments participants in blocks according to date of consent and group start date so that the assessment timeline is consistent between treatment and control subjects.

4. 2-21-14:
   We requested to record the C-SSRS assessment with explicit informed consent of the subject so that it can be rated by a blind rater in order to eliminate potential bias and ensure continuous interrater reliability.
5. 4-14-14:
   We detailed our procedures for contacting Veterans enrolled in the study for both treatment sessions and assessment appointments, explicitly noting that we will use both letters and telephone calls to outreach subjects. Our research team utilizes an approach congruent with standard VA NJ mental health care and VA Suicide Prevention Coordinators to maintain engagement with a person-centered, relationship-building approach.
6. 5-8-14:
   We revised inclusion criteria so that a high risk for suicide flag is not a requirement for participation as some Veterans present with suicide risk yet are not administratively flagged by Suicide Prevention.
7. 5-20-14:
   Alejandro Interian, Ph.D. will assume the role of Principal Investigator as Anna Kline, Ph.D., is retiring as of May 30, 2014.
8. 7-22-14:
   We expanded inclusion criteria to include Veterans treated in outpatient programs. We have formulated the criteria to maintain a focus on a sample that has a suicide event or "crisis" and shows recent risk of suicide behavior.
9. 10-6-14:
   We are specifying all methods the study team may use to recruit Veterans receiving services as outpatients at VA NJ, including mailing letters prior to calling, direct referrals by providers, and the ability for interested referred Veterans to contact the study team directly.
10. 12-5-14:
    We propose to offer the mindfulness-based cognitive therapy to control subjects after they have completed one year of study participation. We are also requesting that these veterans receive reimbursement for travel expenses at a rate of .415/mile for treatment group attendance.
11. 6-26-16:
    We added an optional, qualitative assessment for treatment subjects who completed the study to identify common patterns across cases within each category (e.g., positive response, negative response, unengaged).
12. 7-25-17:
    We added a statement to our consent form to address an expected risk, discomfort, or inconvenience of taking part in study: "Because the treatment sessions focus on helping you to deal with some of the difficulties you are having, you may feel distressed or unsettled during a treatment session. If you are feeling unsettled, please let your instructor know so he or she can counsel you." While we recently conducted an analysis of this issue and found low occurrence rates, we felt it prudent to outline in the informed consent document that feeling upset during therapy is natural. Additionally, we clarified language in our study protocol to include licensing information for study staff and clinicians and outline a more detailed and refined protocol for managing emergent suicidal risk.